REMARKS

The Office action dated July 1, 2004 is acknowledged. Claims 1, 3-9 and 11-18 are pending in the instant application. According to the Office action, each of those claims has been rejected. Reconsideration is respectfully requested in light of the following remarks.

Specification

The Examiner has requested that a substitute specification be submitted to place the specification in proper USPTO format. The applicant respectfully requests that the specification be replaced with the substitute specification enclosed herewith. A clean and a marked-up version are enclosed. The applicant notes that the specification amendments included with the preliminary amendment filed December 22, 2000 and second preliminary amendment filed June 21, 2001 have been incorporated in the present substitute specification. The applicant also notes that the section entitled "Cross-Reference to Related Applications" has been added at the beginning of the specification. The applicant respectfully points out that adding this paragraph at this time is appropriate since the international application from which the present U.S. national phase application claims priority was filed before November 29, 2000, and therefore the time periods set forth in C.F.R. 1.78(a)(2)(ii) are not applicable (per C.F.R. 1.78(a)(2)(ii)(C)).

Rejection of Claims 1, 3-9 and 11-18 under 35 U.S.C. 103(a)

Claims 1, 3-9 and 11-18 have been rejected as being unpatentable over any one of U.S. Patent No. 5,683,711 (Fischer et al.) or WO 97/23227 (Cordes et al.) in view of U.S.

Patent No. 5,357,004 (Calton et al.). It is respectfully submitted that these claims in their present form are patentably distinct from the cited prior art references.

According to the Examiner, Fischer et al. teach a transdermal patch comprising estradiol and norethisterone in a supersaturated state in an acrylic adhesive matrix, the viscosity of which can inhibit crystallization of the supersaturated adhesive. The Examiner also states that the reference teaches that the supersaturation is desirable and necessary in order to impart a high thermodynamic activity to drugs which permeate with difficulty.

Also according to the Examiner, Cordes et al. teach a transdermal patch for release of estradiol and progesterone which comprises a backing layer, a protective release liner and an active ingredient pressure sensitive matrix layer containing a combination of estradiol and norethisterone acetate with a crystallization inhibitor. The Examiner further states that the reference teaches that the transdermal patch is the condition which confers to the active ingredients' activity required for a forced diffusion through the skin, even in the absence of an absorption enhancer and could release constant amounts of the drugs during the entire application time of from 3-7 days.

The Examiner acknowledges that the aforementioned two references fail to teach the specific amino group containing polymers such as crystallization inhibitors. In turn, the Examiner relies on Calton et al. which she states teach polyamines used to interfere with the crystal formation and salt deposition in cosmetic formulations. The Examiner concludes that it would have been obvious to one skilled in the art to provide a transdermal drug delivery device comprising a reservoir of acrylic adhesive and

supersaturated with mixture of estradiol and norethisterone and comprises a crystallization inhibitor as disclosed by either Cordes et al or Fischer et al and to replace the crystallization inhibitor by polyamines as disclosed in Calton et al. The Examiner states that motivation for such combination would be provided by the teaching of Calton et al. that polyamines interfere with the crystal formation and salt deposition in pharmaceutical formulations to be able to deliver the useful compounds, with the reasonable expectation of having a transdermal delivery device comprising a reservoir of acrylic adhesive and supersaturated with a mixture of estradiol and norethisterone and comprises polyamines such as crystallization inhibitors that maintain the supersaturated state during storage and deliver the required amount of the hormones to the patient in need with great success.

The applicants respectfully disagree with the Examiner's conclusion and submit that each and every limitation set forth in the present claims are not taught by the cited prior art references, alone or in combination. Referring first to Fischer et al. '711, the reference teaches to add vitamin E or a vitamin E derivative, such as tocopherols, to inhibit recrystallization in a supersaturated transdermal system containing oestradiol and norethisterone acetate (col. 3, lines 58-62; col. 4, lines 3-33; Examples 1 & 7). The applicant respectfully maintains that the crystallization inhibitors of this reference are not polymers. Moreover, it is respectfully submitted that they do not belong in the group of amino group-containing polymers set forth in the claims of the present application.

With regards to Cordes et al., the reference teaches to use octyl dodecanol as a crystallization-inhibiting substance in a transdermal reservoir supersaturated with

oestradiol and norethisterone acetate (page 6, last paragraph – page 7, line 12). The applicants respectfully maintain that octyl dodecanol is not an amino group-containing polymer.

The applicants submit that, as set forth in claim 1 of the present application, the inhibitors are selected from the following groups of chemical compounds: polyaminoamides, polyaminoimidazolines, polyetherurethaneamines, polyamines and polyglucosamines. The applicants further submit that Calton et al. pertains to copolymers of polyaspartic acid (as noted in the Abstract) which are polyamides (Calton et al., claim 1) and not polyamines as suggested by the Examiner in the Office action. The applicants point out that, as can be seen from the formulas shown in claim 1 and at column 5 of Calton et al., these compounds do not include any amino groups. Moreover, the definitions provided by the reference for residues R, R', R'' and R''' do not include any amino groups (see claim 1 of U.S. '004).

The applicants also submit that the polyaminoamides set forth in the present application, for example in claim 1, are different from the polyamides disclosed in Calton et al. Specifically, the polyaminoamides contain multiple secondary amino groups (i.e., $-NH-R^1-NH-R^2-N-$), with R^1, R^2, etc. being alkyl. In addition, polyaminoimidazolines are distinguishable from the polyamides of Calton et al. due to the presence of an imidazoline group. Moreover, polyetherurethaneamines are derived from polyurethanes and nowhere in Calton et al. are such polymers taught or disclosed. Polyamines contain multiple (i.e., primary and secondary) amino groups, such as $NH_2-(CH_2)_3-NH-(CH_2)_4-$

$NH–(CH_2)_3–NH_2$ (spermine). The applicants further submit that nowhere in Calton et al. are polyamines taught or disclosed, nor are polyglucosamines taught or disclosed therein.

The applicants respectfully submit that since none of Fischer et al., Cordes et al. or Calton et al., alone or in combination, teach or disclose the amino group-containing polymers recited in claim 1 of the present application, the combination of the references cannot render the present invention obvious since every feature of the claimed invention is not taught or disclosed by the combination of the cited prior art references. Moreover, the applicant respectfully disagrees with the Examiner's conclusion that it would have been obvious to replace the crystallization inhibitor with polyamines as disclosed by Calton et al., motivated by the teaching of Calton et al. that polyamines interfere with the crystal formation and salt deposition in pharmaceutical formulations. The applicants disagree with this conclusion since Calton et al. discloses only polyamides, and not polyamines, as discussed above. The reference only mentions polyamines as a starting compound for producing the polyamides necessary for the invention of Calton et al. The crystallization inhibitory function that the Examiner mentioned is attributed to the polyamides (col. 5, paragraph 1 of Calton et al.) but not to polyamines which serve only as a starting material for producing the required polyamides. Moreover, it is respectfully submitted that Calton et al. fails to make up for the aforementioned deficiencies of Fischer et al. or Cordes et al. Based on the foregoing arguments and deficiencies of the prior art references, it is respectfully submitted that the obviousness-type rejection be withdrawn.

Conclusion

For the foregoing reasons, it is respectfully submitted that the present application is in condition for allowance, and such action is earnestly solicited. The Examiner is invited to call the undersigned if there are any remaining issues to be discussed which could expedite the prosecution of the present application.

Respectfully submitted,

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